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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/230,463	07/26/1999	DAVID WYNICK	23016.0002	4323

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EXAMINER	
GUCKER, STEPHEN	
ART UNIT	**PAPER NUMBER**
1649	

DATE MAILED: 03/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/230,463	WYNICK, DAVID	
	Examiner	Art Unit	
	Stephen Gucker	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *09 November 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Response to Amendment

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. Any objections or rejections made in a previous Office Action that are not herein reinstated have been withdrawn.

3. Claims 18 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods comprising the use of galanin or N-terminal fragments of galanin, does not reasonably provide enablement for galanin agonists in general for reasons of record and the following. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The disclosure teaches that galanin is a 29 amino acid neuropeptide and that the N-terminal portion of galanin is highly conserved between species. It is also disclosed that the prior art teaches that N-terminal fragments of galanin augment the effect of morphine, and this augmentation was known in the art as an agonistic effect. However, the specification does not provide an adequate written description, examples, or guidance to fully support the use of a galanin agonist for the following reasons. A galanin agonist is any compound that physiologically functions like galanin, *regardless of its structure*. The only known galanin agonists of record at the time of the effective filing date of the instant application (7/24/96) were galanin itself and N-terminal fragments of galanin. The phrase "galanin agonist" includes any compounds, including

non-peptides, that function like galanin. The instant methods encompass the use of any molecule that acts like galanin, therefore the limitation is functional rather than structural. The scope of the compounds used in the instant claims is therefore very broad, because the breadth is unfettered by any structural limitations. But, the relationship between function and structure for biological peptides is poorly understood. Even minor amino acid changes in a small peptide can bring about radical changes in function (see Rudinger, page 3 and Figure 1.2). Rudinger also states that "the significance of particular amino acids and sequences for different aspects of biological activity cannot be predicted *a priori* but must be determined from case to case by painstaking experimental study" (Rudinger, page 6). The breadth of the instant claims captures the use of any galanin agonist that is not envisioned or adequately supported by the specification, and even though the skill of the practitioner is high (Ph.D., M.D.), the full reasonable enablement of the claims, as Rudinger states, requires "painstaking experimental study," which is clearly beyond routine experimentation with no reasonable expectation of success, even for the skilled practitioner. In summation, and for the reasons given above, the specification does not provide an adequate description, any working examples, or sufficient guidance as to what compounds can be used in the methods as enabled galanin agonists, other than galanin and its N-terminal fragments.

Applicant's arguments and declaration filed 11/9/05 have been fully considered but they are not persuasive because the arguments and declaration are in agreement with the scope rejection of record. The rejection of record limits the scope of the claim to methods comprising the use of "galanin and N-terminal fragments of galanin." Applicant

argues, essentially, that there are 6 known galanin agonists (other than galanin itself) in existence as of the instant effective filing date of 1996, made from the N-terminal region of galanin, which the record has already established to be highly conserved (i.e. similar sequence of amino acids) in both chemical structure and function between different species of animals. Because neither Applicant's arguments or the declaration of Dickenson filed 11/9/05 provide any evidence or valid scientific support or reasoning for galanin agonists that do not comprise at least the N-terminal region of galanin, the rejection is maintained. Applicant's arguments drawn to screening assays to discover unknown galanin agonists are unconvincing as the screening assays have been in use for over ten years (effective date of filing), and the only galanin agonists of record comprise the N-terminal region of galanin, so screening assays for galanin agonists do not place the invention into the hands of the public without undue experimentation when the invention is, in fact, a method of treatment using galanin agonists, and such galanin agonists as a broad functional genus are not scientifically predictable in terms of what their chemical structure comprises in general, after over ten years of research work, other than the N-terminal fragments or region of the galanin peptide itself. Since Applicant did not offer any supported opposing viewpoint to the published work of Rudinger, Applicant's allegations that Rudinger is too old a reference is also unconvincing. Rudinger's observations concerning the unpredictability of peptide structure given only the peptide's function remain unrebutted, and "biological activity cannot be predicted a priori but must be determined from case to case by painstaking experimental study" (Rudinger, page 6).

4. Claim 18 is rejected under 35 U.S.C. 102(b) as being anticipated by Luo et al. ("Luo"). Luo describes methods where galanin is administered to treat spinal cord hyperexcitability following sciatic nerve section (abstract and pages 162-163) which produces peripheral neuropathy as taught by the instant Application (pages 11-12 of the instant specification, where an example of sciatic nerve axotomy (otherwise known as section) and upregulation of galanin is disclosed as support for the idea that galanin agonists can be administered to treat peripheral sensory neuropathy).

Applicant's arguments filed 11/9/05 have been fully considered but they are not persuasive because Applicant argues that the Webster's II New Riverside University Dictionary meaning of treatment is "to effect a cure." The Examiner would like to point out to Applicant that the more common definition of treatment is listed by Applicant as definition number one from the same dictionary: "the act or manner of treating." Each patent application stands or falls on its own merits, so Applicant's use of claims from other patents to define the phrase "to effect a cure" is unpersuasive. Luo clearly discloses the act or manner of treating (administration of galanin to damaged peripheral nerve) that is identical to the instant method and is encompassed by the instant claims. Both the instant methods and the prior art methods inherently include the mechanism of nerve regeneration because the galanin used in both methods is the same identical substance and if galanin's inherent properties include stimulating nerve regeneration when applied to damaged peripheral nerves, the prior art anticipates the instant invention, regardless of whether there is an explicit disclosure in the prior art of all the inherent properties of the administered galanin. The actual method or process step of

administering the galanin is the same in both the instant invention and the prior art reference (Ex parte Novitski, 26 USPQ 1391), so Applicant is unpersuasive in her argument that "[t]he Examiner has provided no technical reasoning to reasonably support the determination that galanin was used as a treatment following peripheral nerve damage in...Luo et al. (bottom of page 8 of arguments filed 11/9/05).

Finally, the Zigmond declaration filed 7/1/04 has been fully considered but is not persuasive because the declaration is drawn to limitations not recited in the claim. The claim is not limited to peripheral administration of galanin, nor does the claim limitation exclude the use of galanin to treat peripheral nerve damage that concomitantly produces neuropathic pain. Furthermore, there are no limitations in the claim as to what comprises "nerve regeneration" while Applicant's arguments and declaration are drawn to observable, complete and full regeneration. Nerve regeneration as recited in the instant claim encompasses the preliminary beginnings of regeneration up to and including its full completion and expression, and nothing persuasive is provided by Applicant's arguments or declaration that nerve regeneration does not begin within a few minutes or hours of administering galanin, absent any evidence of record to the contrary.

5. Claims 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang et al. ("Zhang") for reasons of record and the following. Zhang discloses that the findings in rat concerning galanin are valid and applicable in primates as well.

> "The main reason underlying our experiments was to explore whether the peptide galanin is upregulated in primates as it is in rats, since we have proposed that galanin may represent an endogenous analgesics compound activated after peripheral nerve lesions. Consequently, galanin agonists should represent new

> pharmacological tools to suppress chronic pain. The present findings show that, since some of these mechanisms also operate in monkey, this hypothesis is valid also for primates and provide a further impetus to test galanin or galanin agonists in humans" (page 375 of Zhang).

Zhang does not carry out the experiments that he explicitly suggests. However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use galanin as a treatment following peripheral neuropathy as taught by Zhang, for therapeutic purposes, because Zhang explicitly makes the suggestion to do so. Note that Zhang, in the context of peripheral nerve lesions (i.e. damage), makes the explicit suggestion that "galanin agonists should represent new pharmacological tools to suppress chronic pain" (underlining mine). Chronic pain in humans clearly implies the repeated use of galanin over a period of time that spans weeks, months, even years (the Zhang study was performed over a period of two weeks time). Therefore, the reference renders *prima facie* obvious a method to use galanin agonists to treat peripheral neuropathy, and to extend the use of galanin agonists in humans to treat chronic pain from peripheral nerve lesions, as suggested by Zhang. The repeated, chronic use of galanin agonists in humans as suggested by the prior art to treat chronic pain would result in the galanin agonists promoting nerve regeneration, as required by the limitations of the instant claims. The promotion of nerve regeneration occurring by the chronic use of galanin to treat chronic pain is also supported by Applicant's arguments and affidavits that are directed to nerve regeneration occurring with the use of galanin over a period of time such as 24 hours and beyond, as measured by such phenomenon as retrograde axonal transport of galanin.

Applicant's arguments filed 11/9/05 have been fully considered but they are not persuasive because Applicant argues that many pain-treating compounds do not promote nerve regeneration. However, the Zhang reference discloses the same evidentiary support for the instant invention as the instant specification does: namely, that following peripheral nerve axotomy, levels of galanin increase in response to the lesion. Given that the prior art reference and the instant disclosure teach the identical finding, Applicant's arguments are unconvincing because they encompass compounds such as aspirin, while the prior art reference is clearly dead on point because it provides motivation to use galanin itself as a method of chronic treatment for peripheral neuropathy.

7. No claim is allowed.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technical Center 1600 general number which is (571) 272-1600.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Gucker whose telephone number is (571) 272-0883. The examiner can normally be reached on Monday to Friday from 0930 to 1800. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, can be reached at (571) 272-0867. The fax phone number for this Group is currently (571)-273-8300.

SG

Stephen Gucker

March 7, 2006

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER